

FIG. 1A-1

	Signal peptide	
MMP-1	MHSFPPLLLLFWG-----VVSHSFP-----	ATLETO
MMP-2	MEALMARGALTPRLALCLLCLLSHAAA-----AP-----	SPIIKFPG
MMP-3	MKSLPILLLLCVAV-----CSAYP-----	LDGARAGE
MMP-7	MR-LTVLCVACLL-----PGLALP-----	LPQE
MMP-8	MFSLKTLPLFLLLH-----VQISKAF-----	VSSK
MMP-9	MSLWQPLVLVLVIGCC-----FAAPRQOSTLVIFPG	
MMP-10	MMHLAFLVLVLCIPV-----CSAYP-----	LSGAKEE
MMP-11	MAPAAWLRSAAARALLPPMLLLQLPPPLARALP-----	
MMP-12	MKFLILLLQ-ATA-----SGALP-----	LNSSTSL
MT-MMP-1	MSPAPRPSCLLPLLLTGLTALASLGSQAQSSFSF-----	
MT-MMP-3	MILLTFSTGRRUDFVH-----HSGVFFLOTLMLWILCATVCG	
Consensus	M..L..L....L.....A..P.....	
	Pro-peptide	
MMP-1	DAETIKVMKQRCGVPDVAQ-----FVLTEGNPRWEQTHLT	
MMP-2	DQNTIETMRKRCGNPDVAN-----YNFFPRKP KWDKNQIT	
MMP-3	DSDTLEVMRKRCGVPDVGH-----FRFPFGIP KWRKTHLT	
MMP-7	NSRVIEIMQKRCGVPDVAE-----YSLFPNSP KWT SKVT	
MMP-8	NEETLDMMKRCGVPDSSG-----FMLTPGPN KWERTNLT	
MMP-9	DSATLKAMRTPRCGVPDLGR-----FQTFEGDLKWHHNIT	
MMP-10	DTDTLEVMRKRCGVPDVGH-----FSSFP GMP KWRKTHLT	
MMP-11	APRPASSLRPRRCGVPDSD-GLSARNRQRKRVLSGG--RWEKTDLT	
MMP-12	DTSTLEMMHAPRCGVPDLHH-----FREMPPGP VWRKHYIT	
MT-MMP-1	DADTMKAMRRPRRCGVPDKFGAEIKANVRKRKYATQ-G-LKWQHNEIT	
MT-MMP-3	DRNTIDWMKKPRCGVPDQTRGSSKFHRRKRYALTQ--KWQHKHIT	
Consensus	D..TL..MRKRCGVPD...-----F....PG.PKW.....	

↑ IS-1

FIG. 1A-2

Pro-peptide

EQVDLVQKYLEKYNLKNDGROVEKRRNSGPVV-EKLKMQQEFFGLKVTGKP 79
 DVAPK-TDRELAVQYLNTF-YGCPKE-SCNLFVLKDTLKKKQKFFGLPQTGD 89
 DTSMNLQKYLENYDLKDKVKQFVRKDSGPVV-KKIREMQKFLGLEVTGKL 79
 AGMSLQWEAQDY-LKRFYLYDSETKNANSL-AKLKEMQKFFGLPITGML 74
 EKNTKVQDYLEKFYQLPSNQYQSTR-KNGTNVIVEKLEMQRFFGLNVTGKP 78
 DLRTNLTDRQLAEELYRYGYTRVAEMRGESKSLGPALLLQKQLSLPETGEL 86
 DSNKDLAQYLEKYNLKNDKVKQFRK-DSNLIV-KKIQGMQKFLGLEVTGKL 78
 -----PDVHHLHAERRGPQ-----PWHALPSSPAPAPATQE 67
 KNNVLFGERYLEKFYGLEINKLPVTMKYSGNMKEKIQEMQHFLGLKVTGQL 79
 -----EAWLQQYGYLPPGDLRTHTQRSPOSLS-AAIAAMQKFGYGLQVTGKA 80
 TEQYFNVEWLQKYGLPPTSPRMSVWRSQETMQ-SALAAQQFYGINNTGKV 88
L...Y.L.....-KL..MQKF.GL.VTGKL 100

Catalytic

YRIENYTPDLPRADVDDHAIEKAFQLWSNVTPLTFTKV-----SEGOADIM 160
 YRIIGYTPDLDPEIVDDAFARAFQVWSDVTPLTRFSRI-----HDGEADIM 170
 YRIVNYTPDLPDKDAVDSAVEKALKVWEVTPLTFSRL-----YEGEADIM 160
 YRIVSYTPDLPHITVDRIVSKALNMWGKEIPLHFRKV-----VWGTADIM 155
 YRIRNYTPQLSEAEVERAIKDAFELWSVASPLIFTRI-----SQGEADIN 159
 YWIONYSEDLPRAVIDDAFARAFALWSAVTPTFTVR-----YSRDADIV 167
 YRIVNYTPDLPKDAVDSADIAEKALKVWEVTPLTFSRL-----YEGEADIM 159
 YRILRFPWLQVQVQROTMAEALKVWSDVTPLTFTFV-----HEGRADIM 156
 YRIINNYTPDMNEDVDYAIRKAFQVWSNVTPLKFSKI-----NTGMADIL 160
 FCIONVTPKGEYATYEAIRKAFRWESATPLRFREVPYAIRREGHEKQADIM 178
 YSIKNVTPKVGDPETKAIRAFADVQNVNTPLTFTFEEVPYSELENGK-RDVIDP 185
 YRI.NYTPDL....VD.AI.KAF.VWS.VTPTFT..V-----G.ADIM 200

↑ IS-2

FIG. IB-1

	Catalytic
MMP-1	ISFVRGDHRDNSPFDGPGGNLAHAFQPGPGIGGDAHFDEHERWTN-NFTEYN
MMP-2	INFRWEHGDGYPFDGKDGILLAHAFAPGTGVGSDSHFDDDELWTLCGEQVVR
MMP-3	ISFAVREHGDFYPDGPNGVLAHAYAPGPGINGDAHFDDDEQWTK-DITGIN
MMP-7	IGFARGAGDSYPFDGPGNTLAHAFAPGTGLGGDAHFDEDERWTDGSSLGIN
MMP-8	IAFYQRDHGDNSPDGPNGIILAHAFQPGQGIGGDAHFDAEETWTN-TSANY
MMP-9	IQGVAEHGDGYPFDGKDGILLAHAFPPGPGIQGDAHFDDDELWSLKGVVVP
MMP-10	ISFAVKEHGDFYSPDGPGHSLAHAYPPGPGLYGDIHFDDDEKWT-E-DASGTN
MMP-11	IDFARYWDGDDLFPDGPGGIILAHAFPPKTHREGDVHFYDETWITGDDQGTD
MMP-12	VVFARGAHGDFHAFDGKGGIILAHAFPGSGIGGDAHFDEDEFWTT-HSGGTN
MT-MMP-1	IFFAEGFHGDSSTPFDGEGGFLAHAYFPGPNIGGDTHEFSAEPWTV-RNEDLN
MT-MMP-3	IIFASGFHGDSSPFDGEGGFLAHAYFPGPGIGGDTHEFSDPEPWTGLGNPHDG
Consensus	I.FA....HGD..PFDGPGG.LAHAF.PGPGIGGDAHFD.DE.WT.-.....N
	Catalytic
MMP-1	-----
MMP-2	YGFCPEALFTMGNAEQPCKFPFRFQGTSDYDSCCTTEGRTDGYRWCCTTD
MMP-3	-----
MMP-7	-----
MMP-8	-----
MMP-9	FGCPSERLYTRDGNADGKPCQFPFIFQGQSYSACTTDGRSDGYRWCATTAN
MMP-10	-----
MMP-11	-----
MMP-12	-----
MT-MMP-1	-----
MT-MMP-3	-----
Consensus	-----

FIG. IB-2

VKYNADGEYCKFPFFLNKEYNSCTDGRSDGLWCSTTYNFEKD GK 211
----- 270
----- 211
----- 207
TRFGNADGAACHFPFFIEGRSYSACTDGRSDGLPWCSTTANYD TDDR 210
----- 267
----- 210
----- 208
----- 211
----- 229
----- 237
----- 300

YDRDKKYGFCPETAMSTV-GGNSEGAPCVFPFTFLGNKYESCTSA GR S 211
----- 369
----- 211
----- 207
YDRDKLFGFCPTRADSTVMGNSAGELCVFPFTFLGKEYSTCTSE GR G 210
----- 367
----- 210
----- 208
----- 211
----- 229
----- 237
----- 400

FIG. IC-1

	Catalytic
MMP-1	-----LHRVAA-HELCHSLGLSHST
MMP-2	DGKMWCATTANYDDDRKKGFCPDQGYSLFLVAA-HEFGHAMGLGHSQ
MMP-3	-----LFLVAA-HELCHSLGLFHSQ
MMP-7	-----FLYAA-HELCHSLGLGHS
MMP-8	-----LFLVAA-HEFGHSLGLAHS
MMP-9	DGRLWCATTSNFSDKKKGFCPDQGYSLFLVAA-HEFGHALGLDHS
MMP-10	-----LFLVAA-HELCHSLGLFHS
MMP-11	-----LLOVAA-HEFGHVLGLQHTT
MMP-12	-----LFLTAV-HELCHSLGLGHS
MT-MMP-1	-----GNDIFLVAV-HELGHALGLEHSS
MT-MMP-3	-----NDLFLVAV-HELGHALGLEHSS
Consensus	-----LFLVAA-HE.GHSLGL.HS.
	Hinge
MMP-1	-----RSQNP
MMP-2	-----ASPDIDLGTG
MMP-3	-----PPDSPETPLVPTG
MMP-7	-----
MMP-8	-----LSSNP
MMP-9	APPTVCGPTGPPTVHPSERPTAGTGPPTSAGPTGPPTAGPSTA-TTVP
MMP-10	-----PPASTEELVPTK
MMP-11	-----QPWPTVTSRTPALGPQAGIDTNE
MMP-12	-----DPKENQRL
MT-MMP-1	-----GESGFP TKMPQPRITTSRSPV
MT-MMP-3	-----SPDKIPPTPRLPVPPHRSITPPADPRKNDRPKPPRPPT
Consensus	-----

FIG. IC-2

Hinge	
DIGALMPSY-TFS--GDVQLAQDD-IDGIQAIYG----	261
DPGALMAPIY-TYT--KNFRLSQDD-IKGIQELYG----	446
NTEALMPLYHSLDTRFLRSQDD-INGIQSLYG----	264
DPNAVHYPTYGN-GDPQNFKLSQDD-IKGIQKLYGKRSNRKK----	267
DPGALMYPNYA-FRETSNYSLPQDD-IDGIQAIYG----	262
VPEALMYPMY-RTE--GPRLHKDD-VNGIRHLYGPRPEPRPTTTTPQT	462
NTEALMPLYNSFTELAQFRLSQDD-VNGIQSLYG----	263
AAKALMSAFYT-FRYPL--SLSPDD-CRGVQHLYG----	258
DPKAVMEPTYK-YVDINTFRLSADD-IRGIQSLYG----	263
DPSAIMAPFYQ-WMDTENFVLPPDD-RRGIQQLYG----	284
DPTAIMAPFYQ-YMEQ-TLQLPND-YYR-HQ-RYM----	288
DP.ALMYP.Y.....F.LSQDD-I.GI.Q.LYG----	500
Hemopexin	
VQPI-GEQTPKACDSKLTFDAITIRGE-VMFFKDRFYMRNTNPFY--PEVELN	315
PTPTLGEVTPEICKQDIVFDGIAQIRGE-IFFFKDRFIWRTVTTRDKPMG-PL	507
FVPP-EPGTPANCDPALSFDAVSTLRGE-ILIFKDRHFWRKSLRK--LEPELH	327
----	267
IQPT-GESTPKCPDPSLTFDAITTLRGE-ILFFKDRFYWRRHPQL--QRVEMN	316
LSPVDD----ACN-VNIFDAIAEI-GNQLYLFKDGKYWRFSEGRSRPQGF	554
SVPS-GSEMPAKCDPALSFDAISTLRGE-YLFFKDRFYWRRSHWN-PEPEFH-	326
IAPLEDDAPPDACE--ASFDAVSTIRGE-LFFFKAGFVWRLRGQQL-QPGYPA	330
PNPD--NSEPALCDPNLSFDAVTTV-GNKIFFKDRFFWLKVSERP-KTSVN-	319
DKPKNTYGPNICD--GNFDTVAMLRGEMFVFKK-RWFWRVRNNQVMDGYPM-	355
GRPSYPCAKPNICD--GNENTLAILRREMEVF-KDQWFWRVRNNRV-MDGYPM	376
..P.-.....P..CD.....FDA..T.RGE-..FFKDR.FWR.....	600

FIG. ID-1

	Hemoexin
MMP-1	FTSVFWPQLPNGLEAAVEFADRDEVRFTKGNKYWAV-QGQNVHLGYPKDIYSSFGFPR
MMP-2	LVATFWPELPKIDAVYEAPOEKAVFAGNEYIY-SASTLERGYPLTS-LGLPP
MMP-3	LISFVWPSLPSGVDAAYEVTSKDLVFIKGNQFWAI-RGNEVRAGYPRGIHT-LGFPP
MMP-7	FTSLFWPSLPTGICQAAYEDFDRDLFLFKGNQYWAL-SGYDILQGYPKDISN-YGFPS
MMP-8	LIADKFWALPKKLDVSFEPLSKLFFFSGRQWVYTGASVL--G-PRRLDK-LGLGA
MMP-9	LISAFWPSLSYLDAAEVNSRDVFIKGNQFWAI-RGNEVQAGYPRGIHT-LGFPP
MMP-10	LASRHWQGLPSPVDAAFE-DAQGHWFQGAQYWYV-DGEKPVLG-PAPLTE-LGLVR
MMP-11	LISLWPTLPSGIEAAEIEARNQVLFKDDKYWLI-SNLRPEPNYPKSIHS-FGFPR
MMP-12	PIGFWRGLPASINTAYERKDGKVF-FKGDKHWF-DEASLEPGYFKHIKE-LGRGL
MT-MMP-1	QITYFWRGLPPSIDAVYENS DGNFVF-FKGNKYWVF-KDTLQPGYPHDLIT-LGSGI
MT-MMP-3	LIS.FWP.LP...DAAYE.....VF.FKGN.YW.....GYP.I.I.-LG.P.
Consensus	
	Hemoexin
MMP-1	MIADFPGIGHKVDVFMKDGFF--YFFHGTROYKFDPKT-KRILTL-QKANS-WFNC
MMP-2	LIADAWNAI PDLNLDVVDLQGGGHSYFFKGYLKLKENS-LKSVKF-GSIKSDWLGC
MMP-3	QIAEDFPGIDSKIDAVFEFEGFF--YFFTGSQLEFDNA-KKVTHT-LKSNS-WLNC
MMP-7	-----
MMP-8	SISGAFPGIESKVDVAFQOEHEFF--HVESGPRYYAFDLIA-QRVTRV-ARGNK-WLNC
MMP-9	EVDRMFPGVPLQTHDVFYQREKA--YFCQDFYWRVSSRSELNQVDQGVYTYDILQC
MMP-10	LIADDFPGVPEKVDVLAQAFGFF--YFFSGSSQFEFDNA-RMVTHI-LKSNS-WLHC
MMP-11	R-ATDWRGVPSIDAFAQADQGYA-YFLRGLYWKFDPVK-VKALEGFPRLVGPDFFG
MMP-12	LI TKNFOGIGPKIDAVFYSKNKY--YFFQGSNQFEYDFLL-QRITKT-LKSNS-WFGC
MT-MMP-1	NIKWE-GIPESPRGSMGSDVFTFYKGNKYWKNQKLKVEPGYKPSALRDWMGC
MT-MMP-3	PI TVWK-GIPESPOGAFVHKENGFTFYFKEGVLEIQITRYSRLEPGHPRSLDKDLSC
Consensus	.I..f.GI....DAVE.....-YFF.G....FD.....-.....-W..C

FIG. ID-2

TVKHIDAA-LSEENTGKTYFFVANKYWRDYDEYKRSMDPGYPK 413
 DVQRVDAA-FNWSKNKKTYIFAGDKFYRYNEVKKKMDPGFPK 604
 TVRKIDAA-ISDKEKNKTYFFVEDKYWRFDEKRNSMEPGFPK 424
 ----- 267
 SVOAIDAA-VFYRS--KTYFFVNDQFWRYDNQRQFMEPGYPK 411
 DVAQVTGA-LRSGR-GKMLLFSGRRLWRFEDVKAQMVDPKRSAS 648
 TIIRKIDAA-VSDKEKKKTYFFAADKYWRFDENSQSMEOGFPK 423
 FP--VHAALVWGPEKNKIYFFRGRDYWRFPSTRRVDSPVPR 424
 FVKIDAA-VFNRFYRTYFFVDNQYWRDYDERRQMDGYPK 416
 PTDKIDAA-LFWMPNGKTYFFRGNKYRYFNEELRAVDSEYPK 451
 PPHGIDSA-IWVEDVGKTYFFKGDYRYWRYSEEMKTMDPGYPK 472
 .V..IDAA-.....KTYEF....YWR.DE....MDPG.PK 700

RKN----- 469
 ----- 660
 ----- 477
 ----- 267
 RYG----- 467
 PED----- 707
 ----- 476
 CAEPANTFL----- 488
 ----- 470
 PSGRPRDEGTEETE-VIIIEVDEEGGAVSAAAVLPVLL 549
 DGPTDRVREGHSPDDDIVIKLDNTASTVKATAIVIPCILA 571
 ----- 800

↑ IS-3

FIG. 1E

MMP-1	-----	469
MMP-2	-----	660
MMP-3	-----	477
MMP-7	-----	267
MMP-8	-----	468
MMP-9	-----	708
MMP-10	-----	476
MMP-11	-----	489
MMP-12	-----	470
MT-MMP-1	LLVLAVGLAVFFRRHGTPRRLLYCQRSLDKV	582
MT-MMP-3	LCILLVYTVFQFKRKGTPRHILYCKRSMQEWV	604
Consensus	-----	833

FIG. 2

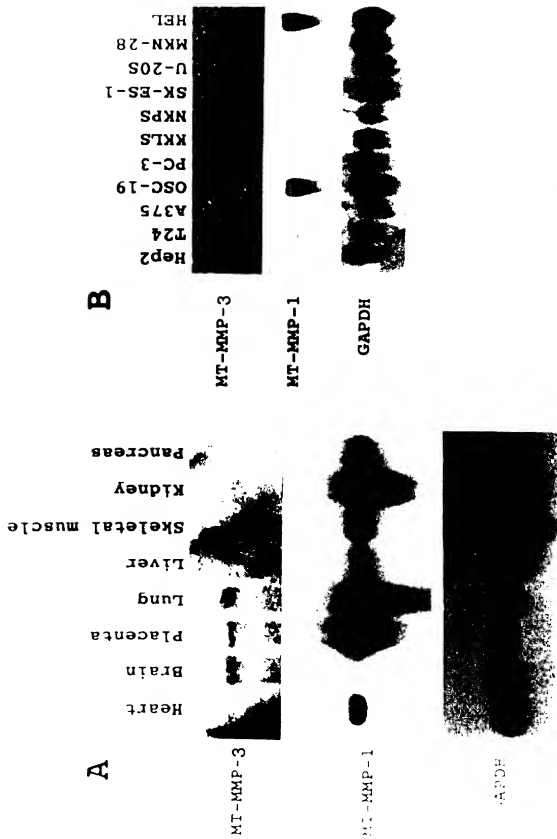


FIG. 3

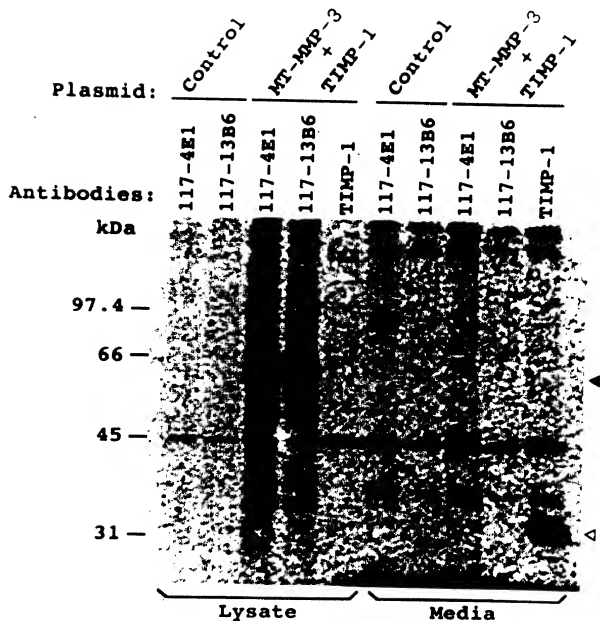


FIG. 4

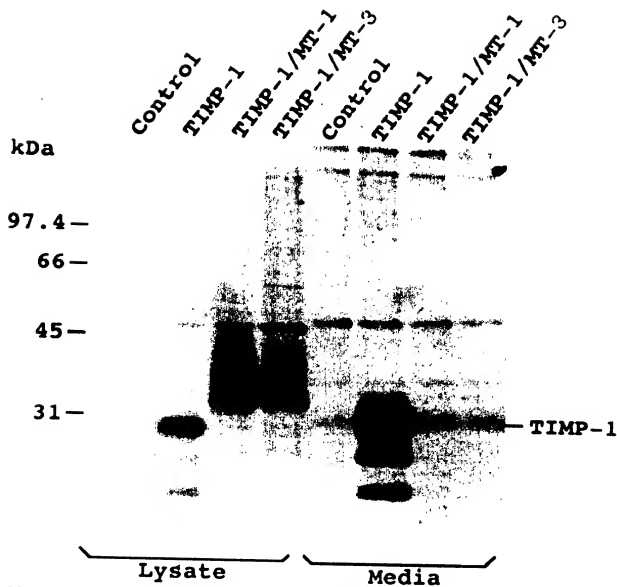


FIG. 5

Control



TIMP-1/MT-3



FIG. 6

